REMARKS

The presently claimed invention concerns a specific compound called LIV-1 (claim 63), a pharmaceutical composition comprising the compound (claim 65) and the use of the compound in the treatment of hepatocellular carcinoma (claim 64). Applicants appreciate the notification that claim 64 is allowed.

Obviousness-type Double Patenting

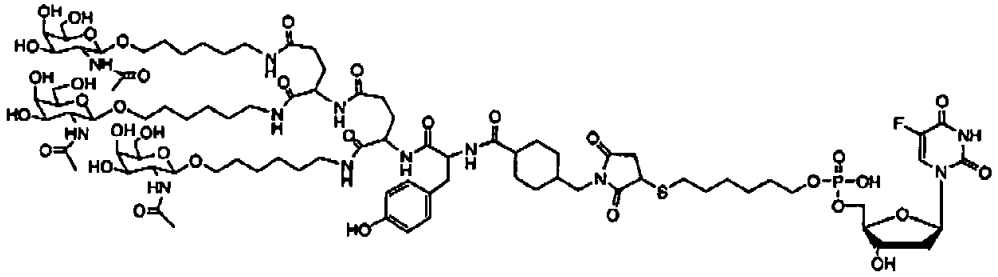
The Examiner rejected claims 63 and 65 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claim 1 of U.S. Patent No. 5,994,517 ("the '517 patent"). Applicants respectfully traverse this rejection.

As the Examiner pointed out in his remarks, the doctrine of obviousness-type double patenting is a doctrine intended to prevent the "unjustified or improper timewise extension of the 'right to exclude' granted by a patent." Such a rejection is warranted when the subject matter of a claim in an application is not "patentably distinct" from the subject matter claimed in a commonly owned patent.

As the MPEP explains, in determining whether an obviousness-type double patenting rejection is warranted, "the first question to be asked is – does any claim in the application define an invention that is merely an obvious variation of an invention claimed in the patent." M.P.E.P. 304 (II) B (1). As explained in greater detail below, it is applicants' position that the presently rejected claims are patentably distinct from the claimed subject matter of the '517 patent because presently rejected claims do not define an invention that is "merely an obvious variation of an invention claimed" in the '517 patent.

The Examiner has rejected currently pending claim 63, below, over claim 1 of the '517 patent.[1]

63. A compound having the formula



The compound of claim 63 is a molecule that includes a glycosylated peptide which recognizes the asialoglycoprotein receptor, a non-peptide linker, and a single molecule of 5FdU, a type of nucleotide. The compound of claim 63 can bind to an asialoglycoprotein receptor on a liver cell and deliver 5FdU to the liver cell.

Claim 1 of the '517 patent reads as follows (emphasis added).

> 1. A delivery system comprising a homogeneous conjugate of formula
> A--L--P
> wherein
> A represents a carbohydrate ligand which binds specifically to a hepatic receptor, thereby facilitating the entrance of said conjugate into cells having said receptor,
> L represents a bifunctional linker that is chemically combined with A and P in a regiospecific manner, and
> P represents a biologically stable oligonucleotide or oligonucleotide derivative, wherein P is released from the conjugate following hydrolysis or reduction of specific biochemical linkages and contains internucleotide linkages

[1] Claim 65 has been rejected together with claim 63. Since claim 65 is drawn to a pharmaceutical composition comprising the compound if claim 63, applicants will discuss only claim 63. However, it is to be understood that the argument made with respect to claim 63 also apply to claim 65.

resistant to enzymatic hydrolysis or biodegradation upon release from the conjugate

wherein A, L, and P are covalently linked.

The conjugate of claim 1 of the '517 patent includes a carbohydrate ligand that binds a hepatic receptor, a linker, and a biologically stable oligonucleotide or oligonucleotide derivative. Significantly, claim 1 specifies that oligonucleotide has internucleotide linkages that are resistant to enzymatic hydrolysis or biodegradation upon release from the bioconjugate.

It is clear that that conjugate of claim 1 of the '517 patent differs substantially from the compound of claim 63. First, the conjugate of claim 1 of the '517 patent includes an oligonucleotide or oligonucleotide derivative. Thus, the conjugate of claim 1 includes a chain of covalently linked nucleotides or derivatives, not a single nucleotide. Moreover, the oligonucleotide or oligonucleotide derivative is specified to have internucleotide linkages that resistant to degradation. Obviously in the case of the compound of present claim 63 there are no internucleotide linkages of any type, much less ones that are resistant to degradation.

It is applicants' position that the compound of claim 63 is not an obvious variant of the conjugate of claim 1 of the '517 patent and thus should not be subject to an obviousness-type double patenting rejection. First, the oligonucleotide portion of the conjugate of claim 1 of the '517 patent differs substantially from the 5FdU portion of the molecule of claim. An oligonucleotide is capable of sequence-specific binding to another nucleic acid molecule. Thus, an oligonucleotide can act as an gene-specific antisense molecule. In contrast, a single nucleotide such as 5FdU is not capable of sequence specific binding and therefore cannot act as gene-specific antisense molecule. Second, there is a substantial size difference between a oligonucleotide and a single nucleotide in that even the smallest molecule that could conceivably be considered an oligonucleotide, a 2 mer, is twice the size of a single nucleotide. Many oligonucleotides, of course, are much larger, particularly those intended to bind to a nucleic acid molecule in a sequence specific manner.

Given the significant differences between the conjugate of claim 1 of the '517 patent and the compound of claim 63, a finding of obviousness requires both: 1) a clear suggestion to modify the conjugate of claim 1 of '517 patent and 2) a clear motivation to make the modification. No suggest suggestion or modification is present. Quite to the contrary, claim 1 of the '517 patent actually teaches away from conjugates that includes a single nucleotide. This is evident from the fact that claim 1 specifies that the oligonucleotide have internucleotide linkages are resistant to degradation. Thus, the claim emphasizes retaining a covalently linked chain of nucleotides and the there is nothing to teach or suggest modifying the conjugate of claim 1 to include a single nucleotide. For at least these reasons, the molecule of claim 63 cannot be seen as a trivial or obvious variant of the conjugate of claim 1 of the '571 patent.

It is also applicants' position that the granting of claim 63 of the present application cannot be reasonably seen as permitting an improper timewise extension of the right to exclude conferred by the grant of claim 1 of the '517 patent. As discussed above, claim 1 of the '517 patent specifies the inclusion of an oligonucleotide or oligonucleotide derivative having a certain type of internucleotide linkage. Given the differences in subject matter, the grant of claim 63, which is drawn to a molecule having a single molecule of 5FdU and has no internulceotide linkages of any type cannot reasonably be seen as extending the rights of claim 1 of the '517 patent.

In view of the forgoing, applicants respectfully request that the rejection of claims 63 and 65 under the judicially created doctrine of obviousness-type double patenting be withdrawn and the claims passed to allowance.

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Enclosed is a Petition for Extension of Time and a Notice of Appeal with authorization to charge fees to Deposit Account. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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